Effect of short-term monotherapy with UK-427,857 on viral load in HIV-infected patients

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Background: UK-427,857, is a CCR5 antagonist with potent anti-HIV activity *in vitro*. A study to evaluate the effect of short-term monotherapy on viral load and the relationship between viral load reduction, plasma drug concentration and CCR5 receptor saturation is being conducted in HIV patients.
Methods: In a first part of the study, 24 asymptomatic HIV positive patients with CD4 count >250 cells/mm^3 and plasma viral load >5000 copies/ml received UK-427,857 25mg QD, 100mg BID or placebo for 10 days and were followed up until day 40. Patients were pre-screened for the presence of CCR5-tropic virus only. Viral load, UK-427,857 plasma concentration, and CCR5 receptor saturation were evaluated at regular intervals throughout the study. Clinical safety evaluations, including ECGs and laboratory safety tests were also performed.
Results: UK-427,857 was well-tolerated with no severe or serious adverse events recorded. Plasma concentrations were similar to those seen in healthy volunteers under similar food restrictions, with all patients receiving 100mg BID reaching trough concentrations in excess of the mean antiviral IC_{90} in PBMC at steady-state. Mean CCR5 receptor saturation at 100mg BID was in excess of 90% throughout the dosing period, but at 25mg QD mean saturation fell to <80% by day 10. CCR5-tropic patients receiving 100mg BID had a mean decrease in viral load of 1.42 $\log_{10}$ from baseline to day 11, with a mean decrease of 0.42 $\log_{10}$ seen for 25mg QD.
Conclusion: UK-427,857 100mg BID was well tolerated and exhibited potent antiviral effects when given as short-term monotherapy. These results indicate that further evaluation of UK-427,857 for the treatment of HIV infection is merited.